



NTP
National Toxicology Program

Workshop Concept
Exposure to Permanent Hair Dyes and Cancer:
Needs and Approaches for Improved Hazard
Characterization

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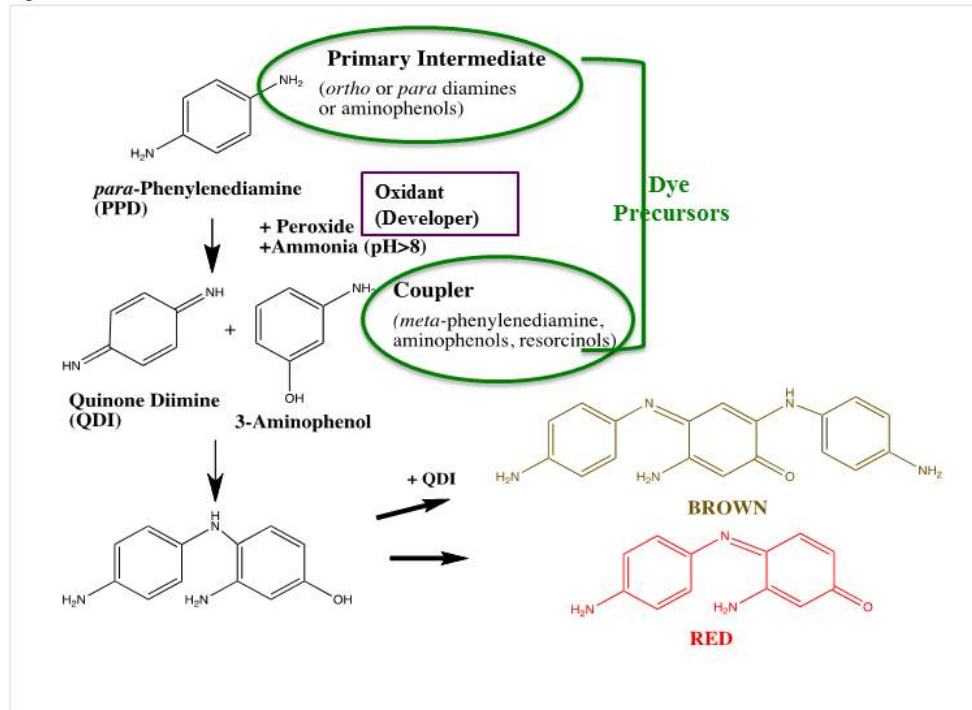
The public is concerned about the safety of hair dyes

- Millions of people in the U.S. and Europe use hair dyes
- The questions of whether hair dyes cause cancer, and what types of dyes or products are safe, are one of the most frequent inquiries to the OROC
- Congress expressed concern about mutagens in hair dyes in the 1970's
 - Some hair dyes were taken off the market in the 1980s because they were mutagenic or caused cancer in experimental animals
 - Dyes used today are in the same chemical class as those taken off the market



Permanent hair dyes are the result of chemical reactions between oxidized primary intermediates (colorless dye) and couplers:

Example





Some hair dyes can cause genetic damage and cancer in laboratory animals

- Metabolism of aromatic amines can occur through Phase I and/or Phase II enzymes leading to the formation of nitrenium ion, which can bind DNA, forming adducts and leading to mutations
- NTP has tested 26 chemicals used in hair dyes by gavage or administered in the diet and 1 chemical by dermal administration
 - A few of these are listed as *reasonably anticipated to be a human carcinogen* by NTP or *possibly carcinogenic* to humans by IARC
- IARC concluded there was limited evidence of carcinogenicity of hair colorants from studies in experimental animals. Most of these studies exposed animals using topical application of hair color mixtures, and IARC noted they had methodological limitations



Some studies found an increased risk of cancer among people using hair dyes

- IARC concluded that there was inadequate evidence for the carcinogenicity of personal use of hair dyes from human studies
 - Inconsistent findings for urinary bladder cancer
 - Increased risks for specific subtypes of non-Hodgkin's lymphoma (NHL) in pooled analyses, but no strong exposure-response relationships
 - Increased risks mainly found among people who started using hair dyes prior to 1980s
 - Polymorphisms in metabolizing enzymes (e.g., NAT2) modify cancer risk
- A risk factor for NHL is altered immunity
 - Some hair dyes cause immune effects but the relationship between these effects and NHL has not been adequately explored



State of the science and key issues

- State of the science is unclear
 - Recent (2008) IARC working group concluded that “personal use of hair colourants is not classifiable as to its carcinogenicity to humans”
 - Positive findings in some studies in humans and experimental animals causes some concern, and thus more research is needed
- Key issues in hair dye research are:
 - Large number of chemicals
 - Topical exposure to a mixture of chemicals
 - Variation of dyes across commercial brands and shades
 - Types of dye used changes over time
 - Genetic susceptibility



Advantages of a workshop

- Workshop provides a forum to advance the state of the science and testing strategies
- A focused discussion of data gaps, research strategies and testing methods is needed
- Cross-disciplinary scientific input from public and private sectors for testing and research
- Provides opportunity to evaluate utility of short-term assays [e.g., Tox21] for testing safety of hair dyes
 - No current guidelines in the United States for testing individual hair dyes or commercial hair colorants



Workshop Goals

Identify knowledge gaps in testing and research evaluating hair dyes and cancer risk

Identify approaches to improve (1) toxicity testing of individual dyes and/or commercial products, and (2) epidemiologic studies

Identify and propose mechanisms of cancer induction potentially applicable for hair dyes and research strategies to test them

Foster multi-disciplinary discussions to facilitate the use of toxicology to inform epidemiologic study design



Proposed approach

Pre-workshop

- Workshop planning committee [NIEHS & other government agencies]
- Literature review document
- Selection of participants [multiple disciplines]

Workshop

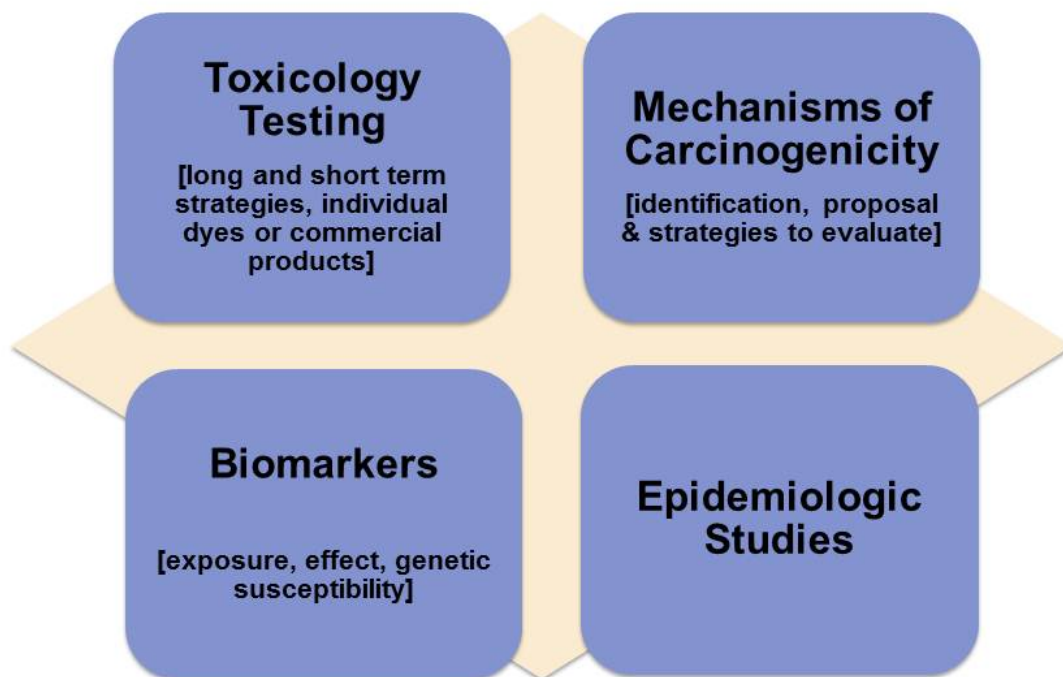
- Plenary sessions, presentations and multiple sequential break-out groups
- Cross-disciplinary discussions and recommendations

Post-workshop

- Final workshop report
- Publications(s) in the peer-reviewed literature



Proposed breakout group topics





Significance and expected outcomes

- Workshop provides a forum for a cross-disciplinary, focused discussion of the path forward to help answer this question on whether hair-dye use in humans is a cancer hazard
- These discussions should stimulate innovative research and testing activities, collaboration, and possibly hazard evaluations
- May lead to targeted testing nominations to the NTP
- The final workshop report and any related publications will be a useful resource to the NTP, NIEHS, other government agencies, European Union, research organizations, and the scientific community